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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/565,417

08/03/2006

William J. Welsh

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11/30/2007

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EXAMINER

SMITH, CAROLYN L

ART UNIT

PAPER NUMBER

1631

NOTIFICATION DATE

DELIVERY MODE

11/30/2007

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No. 10/565,417	Applicant(s) WELSH ET AL.	
	Examiner Carolyn L. Smith	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendments and remarks, filed 10/2/07, are acknowledged. Amended claims 1-4 and cancelled claims 5-8 are acknowledged.

Applicant's arguments, filed 10/2/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-4 are herein under examination.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 4 recites "The computer program of claim 3" which lacks clarity as to whether the claim is intended to only refer to the program or to the computer-readable medium (to which is what claim 3 is actually directed). Applicant is reminded that the dependent claim is to include all the limitations of the independent claim from which it depends; however, the current wording

in claim 4 is confusing regarding this matter. Clarification of this issue via clearer claim wording is requested. This rejection is necessitated by amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Troyanskaya et al. (Bioinformatics, 2001, Volume 17, Number 6, pages 520-525) with additional support from online Merriam-Webster dictionary (“Gaussian” definition). This rejection is maintained and reiterated for reasons of record.

Troyanskaya et al. disclose methods for estimating missing values in DNA microarrays via imputing (abstract and title). Troyanskaya et al. disclose k-means clustering and various model-based approaches and algorithms, such as (Single Value Decomposition) SVDimpute algorithm via normalization for microarray data comprising rows and columns (page 520, col. 2, first and second paragraphs; page 521, col. 1, first and second and fourth paragraphs and col. 2, first and last paragraph). According to the online Merriam-Webster dictionary, the definition of “Gaussian” is “being or having the shape of a normal curve or a normal distribution” (this definition is not being used as prior art, but rather to clarify the definition of the term “Gaussian”). The normalization of data represents normal distributions or Gaussian distributions

or models. Troyanskaya et al. disclose using k eigengenes, using a row average, and an expectation maximization method that is repeated until the change falls below a threshold (converges) (page 522, col. 1, third and fourth paragraphs). Troyanskaya et al. disclose a website, software and methods implemented on a computer (abstract and page 524, col. 1, last paragraph) which represents a computer readable medium and program and computer which inherently contains memory and output of missing values.

Thus, Troyanskaya et al. with additional support from online Merriam-Webster dictionary anticipate the instant invention.

Applicant argues about the normalization described in Troyanskaya et al. refers to a different process in microarray data analysis that does not teach that data are transformed into one normal distribution. Further, Applicant argues the instant method employs Gaussian mixture clustering which imposes a mixture of multivariate normal (Gaussian) distributions. This statement is found unpersuasive as Applicant is arguing limitations not found in the instant claims. Applicant's arguments are deemed unpersuasive for the reasons given above.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1 and 3 are rejected under 35 U.S.C. 102(a) as being anticipated by Hytopoulos et al. (US 2002/0169560 A1) with additional support from online Merriam-Webster dictionary ("Gaussian" definition). This rejection is maintained and reiterated for reasons of record.

Hytopoulos et al. disclose a computer-implemented method and a system using microarray expression data arrays, cluster arrays, and clustering tools wherein the expression values have been normalized, filtered, and imputed, wherein missing data are imputed, and outputted (abstract and paragraphs 0002, 0052, 0084, and 0123). According to the online Merriam-Webster dictionary, the definition of "Gaussian" is "being or having the shape of a normal curve or a normal distribution" (this definition is not being used as prior art, but rather to clarify the definition of the term "Gaussian"). The normalization of data represents normal distributions or Gaussian distributions or models. Hytopoulos et al. disclose using a computer readable medium in association with a computer including a processor and memory and computer instructions which are configured to cause a computer to process data (claim 15) which represents an algorithm and computer software program and product. Hytopoulos et al. disclose allowing the user to select K-nearest neighbor imputation mechanism or other data imputation mechanisms (paragraph 0125). Hytopoulos et al. disclose analysis of gene expression data to form clusters (abstract). Hytopoulos et al. disclose identifying genes represented in respective rows (paragraph 0038) which represents a partitioning of rows of microarray data. Hytopoulos et al. disclose mapping rows of expression data (paragraph 0131). Thus, Hytopoulos et al. with additional support from online Merriam-Webster dictionary anticipate claims 1 and 3.

Applicant argues about the normalization described in Hytopoulos et al. refers to a different process in microarray data analysis that does not teach that data are transformed into one normal distribution. Further, Applicant argues the instant method employs Gaussian mixture clustering which imposes a mixture of multivariate normal (Gaussian) distributions. This statement is found unpersuasive as Applicant is arguing limitations not found in the instant claims. Applicant's arguments are deemed unpersuasive for the reasons given above.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hytopoulos et al. (US2002/0169560 A1) with additional support from online Merriam-Webster dictionary ("Gaussian" definition) in view of Cereghini et al. (US 6,496,834 B1). This rejection is maintained and reiterated for reasons of record.

Hytopoulos et al. describe the limitations in instant claims 1 and 3, as discussed above in the 35 USC 102 rejection. Hytopoulos et al. do not describe repeating a classification expectation-maximization algorithm until the K partitions converge.

Cereghini et al. describe a method of performing cluster analysis inside a relational database management system using Gaussian mixture parameters and implementing an Expectation-Maximization (EM) clustering algorithm iteratively (abstract). Cereghini et al. describe grouping a set of data into k clusters with k rows (partitioned) (col. 2, lines 57-63). Cereghini et al. describe the expectation-maximization algorithm converges quickly and performing iterations (col. 9, lines 34-42).

Hytopoulos et al. state that effective mechanisms for analyzing DNA array data are needed to determine which genes or combination of genes are correlated to various human conditions (paragraph 0009). Cereghini et al. state the EM algorithm is robust for noisy data and missing information (col. 7, lines 5-6). Cereghini et al. state cluster analysis does not typically work well with large databases due to memory limitations and the execution times required (col. 2, lines 32-39). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use effective means for analyzing DNA array data, as stated by Hytopoulos et al., by using algorithms supporting large databases, as stated by Cereghini et al. The person of ordinary skill in the art would have been motivated to make that modification in

order to find effective ways (as stated by Hytopoulos et al. and Cereghini et al.) of correlating genes to human conditions (as stated by Hytopoulos et al.) by allowing non-statisticians to benefit from advanced mathematical techniques available in a relational environment, as stated by Cereghini et al. (col. 2, lines 40-43).

Thus, Hytopoulos et al. with additional support from the online Merriam-Webster dictionary, in view of Cereghini et al. motivate the instant invention.

Applicant reiterates arguments regarding Hytopoulos et al.'s normalization which were already found unpersuasive as discussed above in the 35 USC 102 rebuttal. Applicant argues that Cereghini et al. do not use Guassian mixture cluster to estimate missing values. This statement is found unpersuasive as Hytopoulos et al. was relied on for this limitation in the 35 USC 103 rejection. Applicant's arguments are deemed unpersuasive for the reasons given above.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on (571) 272-0720.

November 20, 2007

/Carolyn Smith/
Primary Examiner
AU 1631